IMPACT OF TESTS ON DIAGNOSTIC AND CLINICAL DECISIONS

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Phased evaluation of medical tests:
Diagnostic thinking efficacy

Proposals for a Phased Evaluation of Medical Tests

Jeroen G. Lijmer, MD, PhD, Mariska Leeflang, PhD,
Patrick M. M. Bossuyt, PhD

Med Decis Making 2009
Why does it matter?

- Why order tests if the results do not make any difference to clinical decisions?

- Test results will have an impact on patient outcomes, provided they correctly guide clinical decisions made by physicians.

Change in physician’s decisions or behavior is an intermediate step for improvement in patient outcomes

A simplistic model
A more complex model

Whatever the test, impact on patient outcomes depends on how the test is ordered, performed, and interpreted.

Doctor orders test → Impact on patient outcomes

Correct test is ordered → Patient gets it done

Doctor acts on the results → Lab performs test well

Results get reported quickly → Results do not get reported in time; no standards; no quality assurance; POC tests are not used at POC

Lab performs test well → Cannot do it well; charges a lot of money; need to give kickbacks to doctors; imported tests are expensive; half-volume testing; kitchen sink testing

Doctor orders inappropriate or inaccurate test → orders unnecessary test for kickbacks; has own lab that needs business

Cannot afford the test; does not believe in testing; unhappy with doctors who ask for tests; wants quick therapy

A very realistic model (in India)

Underuse or overuse of diagnostics; empiricism; access to lab; patient’s SES; easier to give antibiotics; medical training

No impact on patient outcomes

Doctor does not act on the results (quality, lack of trust); has already given empiric therapy

Results do not get reported in time; no standards; no quality assurance; POC tests are not used at POC

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Example: influenza RIDTs

Impact of Rapid Diagnosis on Management of Adults Hospitalized With Influenza

Ann R. Feinley, MD, Yoshihiro Maruta, MD, PhD, Edward E. Walsh, MD

Background: Rapid influenza testing decreases antibiotic and ancillary test use in febrile children, yet its effect on the care of hospitalized adults is uncertain. We compared the clinical management of patients with influenza whose rapid antigen test result was positive (Ag+) with the management of those whose rapid antigen test result was negative or the test was not performed (Ag-).

Methods: Medical record review was performed on patients with influenza hospitalized during winters (1999-2003). Hospital policy mandated influenza testing (antigen or culture) for all patients with acute respiratory tract illness seen from November 13 through April 13. A subset of patients participated in a pharmacological study and had reverse-transcriptase polymerase chain reaction or serologic testing performed. Clinical data from Ag+ and Ag- patients were compared.

Results: Of 166 patients with available records, 86 were Ag+ and 80 were Ag-. Antimicrobial use (78% of 86 patients vs 79% of 80 patients; P = .82) was low and antibiotic discontinuation (12% of 86 patients vs 2% of 80 patients; P = .31) was greater in Ag- compared with Ag+ patients. No significant difference in antibiotic days, length of hospital stay, or antibiotic complications was noted. Antiviral use (49% vs 46%) was greater in Ag+ than Ag- patients. Antiviral status was independently associated with withholding or discontinuing antibiotics in a multivariate analysis. Of 44 Ag+ patients deemed low risk for bacterial infection, 27 continued to receive antibiotics despite positive influenza test results. These patients more commonly had pneumonia, had significantly more abnormal lung examination results (P = .001), compared with those in whom antibiotics were withheld or discontinued.

Conclusions: Rapid influenza testing leads to reductions in antibiotic use in hospitalized adults. Better tools to rule out concurrent bacterial infection are needed to optimize the impact of viral testing.

Arch Intern Med 2007;167:351-360

Example: malaria RDTs

Use of RDTs to improve malaria diagnosis and fever case management at primary health care facilities in Uganda

Daniel N. Kabatereine*, Caroline Kohlmeier*, Damali Nakasakka*, Jane Nakabago*, Helen Coopman* and James K. Utabakama*

Abstract

Background: Early and accurate diagnosis of malaria followed by prompt treatment reduces the risk of severe disease in high-endemic regions. Presumptive treatment of malaria is widely practiced where microscopy or rapid diagnostic tests (RDTs) are not readily available. With the introduction of artemisinin-based combination therapy (ACT) treatment of malaria in many low-resource settings, there is need to target treatment to patients with parasitologically confirmed malaria in order to improve quality of care, reduce over consumption of anti-malarials, reduce drug pressure and reduce drug development and spread of drug resistance. This study evaluated the effect of malaria RDTs on health workers' anti-malarial drug (AMO) prescriptions among patients at low-level health care facilities (LHCF) within different malaria-endemic settings in Uganda.

Methods: All health workers (n = 7) selected intervention where RDTs were deployed. LHCF were invited for training on the use of RDTs. All staff that were trained to use RDTs for parasitological diagnosis of all suspected malaria cases irrespective of age. The LHCF with clinical diagnosis (CD) only were included for comparison. Subsequently AMO prescriptions were compared in pre- test and intervention - control arms analyse data in common measures such as prescription rates, treatment of amodiaquine (ATD), and drug classes.

Results: A total of 10151 test patient attendance (RDTs) were evaluated at 31 intervention LHCFs. Overall use of RDTs in a 28.8% reduction in AMO prescription. There was a 22 fold reduction in RDTs in AMO prescription with the greatest reduction in the hyper-endemic setting (54.5% reduction in ATD prescription). The greatest reduction in AMO prescription represented a significant change in the use of RDTs, with p-value < 0.001. Over eight of all eligible patients were offered a test. An average of 5% change in the AMO prescription between the pre-test and intervention groups. When these groups were compared only patients that had a result were included. The study demonstrated that RDT use in an LHCF, and can lead to better targeting of malaria treatment. Nationwide deployment of RDTs in a systematic manner should be prioritised to reduce the risk of malaria treatment. The process should include plans to educate health workers about the utility of RDTs in order to maximum acceptance and uptake of the diagnostic tools and thereby leading to the benefits of parasitological diagnosis of malaria.
TB EXAMPLE: 
DOES QUANTIFERON-TB GOLD HELP WITH LTBI TREATMENT DECISIONS IN CHILDREN?

Daphne Ling, Claire Crepeau, Marieke Dufresne, Caroline Quach, Larry Lands, Madhukar Pai
McGill University, Montreal

Rationale

Children are at high risk for TB disease, if latently infected

LTBI therapy (INH preventive therapy) is a key intervention to prevent disease

IGRAs are now available for clinical use, but do they influence clinical decisions?
Introduction of QFT at the Montreal Children's Hospital

MEMORANDUM

In summary, the indications for pediatrics are as follow:

1. In support for the diagnosis of active tuberculosis in children (<18 years), in combination with other microbiological tests
2. Children in contact with a case of active infectious tuberculosis with a positive PPD
3. Immunocompromised children defined as:
   a. Receiving Prednisone (2 mg/kg/day) for 14 days or more
   b. Current chemotherapy or received in the past 3 months
   c. Pre or post-bone marrow transplant
   d. HIV positive children
   In whom a clinician is still concerned about the possibility of LTBI even after a negative PPD
4. Patients with inflammatory diseases prior to starting anti-TNF medication

Objective

To prospectively determine the impact of QuantiFERON (QFT) test results on diagnostic and treatment decisions made by pediatric respirologists in routine clinical practice
Methods

- Several subgroups of children were prospectively recruited
- Concordance was calculated for pre-defined subgroups
- A clinical impact questionnaire was used to assess clinical changes based on the QFT (e.g. LTBI → no LTBI)

Subgroups

- Active TB suspects
- TB contacts
- Targeted screenings: TST+, foreign-born children from school-based or immigration screenings
- Immunocompromised children
- TB clinic consults: referrals from other MCH clinics to rule out LTBI (pre-treatment, NTM, etc.)
Clinical impact questionnaire

1. My final diagnosis (after workup):
   - Current TB infection (LTBI)
   - Active TB disease
   - No TB infection or disease

2. Did QFT test play any role in making the above diagnosis?
   - Yes
   - No
   - Not applicable, QFT was not requested or results were not available to me

3. If yes to the above question, how was it useful?

<table>
<thead>
<tr>
<th>Test</th>
<th>QFT</th>
<th>Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST</td>
<td>+</td>
<td>I used the negative QFT to rule out LTBI</td>
</tr>
<tr>
<td>TST</td>
<td>-</td>
<td>I used the positive QFT to diagnose LTBI</td>
</tr>
<tr>
<td>TST</td>
<td>?</td>
<td>I used both positive TST and QFT to diagnose LTBI</td>
</tr>
<tr>
<td>TST</td>
<td>+</td>
<td>I used the negative QFT to rule out active TB</td>
</tr>
<tr>
<td>Other explanation:</td>
<td></td>
<td></td>
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<tbody>
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<td>+</td>
<td>I used the positive QFT to diagnose active TB</td>
</tr>
<tr>
<td>Active TB</td>
<td>-</td>
<td>I used the negative QFT to rule out active TB</td>
</tr>
<tr>
<td>Other explanation:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clinical impact questionnaire

4. If I had not ordered QFT, my diagnosis would have probably been:
   - Current TB infection (LTBI)
   - Active TB disease
   - No TB infection or disease

5. My final treatment decision (after workup):
   - No anti-TB therapy for LTBI
   - LTBI prophylaxis: Not for 6 or 9 months or specify other regimen:
   - Active TB disease therapy

6. Did QFT test play any role in the above treatment decision?
   - Yes
   - No
   - Not applicable, QFT was not requested or results were not available to me

7. If yes to the above question, how was it useful?

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</thead>
<tbody>
<tr>
<td>TST</td>
<td>+</td>
<td>I used the negative QFT to withhold LTBI prophylaxis</td>
</tr>
<tr>
<td>TST</td>
<td>-</td>
<td>I used the positive QFT to initiate LTBI prophylaxis</td>
</tr>
<tr>
<td>TST</td>
<td>?</td>
<td>I used both positive TST and QFT to initiate LTBI prophylaxis</td>
</tr>
<tr>
<td>TST</td>
<td>+</td>
<td>I used the positive QFT to rule out LTBI prophylaxis (regardless of TST result)</td>
</tr>
<tr>
<td>Active TB</td>
<td>+</td>
<td>I used the positive QFT &amp; other signs/assess to initiate anti-TB therapy</td>
</tr>
<tr>
<td>Other explanation:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Signature: ___________________ Date: ___________ Chart #: ___________
Results

- 242 children with TST & QFT results
- Active TB suspects (n=5)
- TB contacts (n=71)
- Targeted screenings (n=120)
- Immuno-compromised children (n=5)
- TB clinic consults (n=35)
- Research samples (n=6)

Results – Clinical Impact

Data on the clinical impact of QFT were available in 119/242 (49%) children who had already returned for their follow-up visit.
Clinical Impact

- TB contacts: In all QFT contacts, the QFT was not used to change clinical decisions. INH was prescribed regardless of the QFT result.

<table>
<thead>
<tr>
<th>TB contacts (n=71)</th>
<th>TST +</th>
<th>TST -</th>
</tr>
</thead>
<tbody>
<tr>
<td>QFT +</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>QFT -</td>
<td>24</td>
<td>21</td>
</tr>
<tr>
<td>QFT indeterminate</td>
<td>2</td>
<td>1</td>
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</table>

Clinical Impact

- Targeted screening: The QFT changed the initial diagnosis from LTBI → no LTBI in 70% of children. INH was withheld or stopped after a while.

<table>
<thead>
<tr>
<th>Targeted screenings (n=120)</th>
<th>TST +</th>
<th>TST -</th>
</tr>
</thead>
<tbody>
<tr>
<td>QFT +</td>
<td>22</td>
<td>X</td>
</tr>
<tr>
<td>QFT -</td>
<td>97</td>
<td>X</td>
</tr>
<tr>
<td>QFT indeterminate</td>
<td>1</td>
<td>X</td>
</tr>
</tbody>
</table>
Follow-up for patient outcomes

- For children not prescribed INH, follow-up with phone call to see if they have developed symptoms consistent with active TB.
- Ongoing, but no TB cases thus far...
- This illustrates the importance of thinking beyond change in decisions to real patient outcomes.
- There are many issues which may confound physician’s behaviors – not easy to capture in research studies.